REMARKS

Objection was made to Fig. 6 as being incomplete. This application is a national stage filing of a PCT application which must meet the drawing requirements of 37 CFR 1.437, which references PCT Article 7 and PCT Rule 11. Section 11.11 of Rule 11 states that text is not to be included in PCT application drawings except for single words or symbols. This is due to translation problems in the many countries with different languages where the international application may be filed. Accordingly, it is respectfully submitted that the "empty box" drawings of Fig. 6 are in compliance with the rules and acceptable. However, for the convenience of the Examiner a replacement sheet for Fig. 6 is enclosed, which is Fig. 6 of the priority provisional application. In this drawing the boxes of the ultrasound system are filled in with their descriptive text.

It is respectfully requested that the Examiner approve entry of the enclosed Replacement Sheet drawing.

Objection was made to the title as not being descriptive, as the claims are directed only to methods. Accordingly the title has been amended to remove the reference to "system."

Claims 3, 5, 9 and 10 were rejected under 35 U.S.C. §1112, second paragraph as being indefinite. In particular, objection was made to the use both "broad beams" and "focused beams" in Claim 5. Claims 3, 9, and 10 have been canceled. The objectionable words in Claim 5 have been replaced with "plane wave" for consistency in both instances. Accordingly it is respectfully submitted that Claim 5 is now clear and definite.

Claims 1, 4, 8, 11 and 12 were rejected under 35 U.S.C. §103(a) as being unpatentable over the prior art description in the present specification and US Pat. 5,577,505 (Brock Fisher). Claim 1 describes a method of obtaining an ultrasound perfusion image of tissues perfused with blood containing microbubbles, the method comprising transmitting a plane wave of microbubble-destroying ultrasound into the tissues, the plane wave of microbubble-destroying ultrasound encompassing a first area of the tissues, the microbubble-destroying ultrasound having an intensity that is sufficient to destroy microbubbles in the tissues that are insonified by the microbubble-destroying ultrasound; repetitively transmitting a plurality of beams of imaging ultrasound into the tissues, each beam of imaging ultrasound having a second area that is smaller than the first area, the imaging ultrasound having an intensity that is substantially insufficient to destroy microbubbles in the tissues that are insonified by the imaging ultrasound; receiving reflections from each of the transmitted

imaging ultrasound beams in respective receive beams, each of the receive beams having a third area that is smaller than the first area; and processing the received reflections over a sufficient period to allow re-perfusion of the tissues to provide an ultrasound perfusion image. The inventive method provides improved accuracy in destruction-replenishment perfusion imaging and the calculation of perfusion curves by using a plane wave to uniformly destroy microbubbles in the image field with one or only a few transmissions. With the microbubbles uniformly destroyed, individual beams are used to interrogate the field as it is reperfused, with the smaller area of the individual beams providing higher resolution needed for accurate imaging and precise perfusion measurements. This is a significant improvement over the standard prior art technique of destroying the microbubbles with individual beams, line by line. As this technique proceeds across the image field, the lines first cleared can begin to reperfuse before destruction of the full field is complete, producing a nonuniform starting point from which to measure reperfusion. The other technique of using plane waves to interrogate the image field lacks the resolution of individual beams thus also suffering from imprecision. The present invention overcomes the drawbacks of both of these approaches.

It is not clear whether Brock-Fisher is doing destruction-reperfusion imaging of microbubbles or is simply imaging microbubbles at low MI without destruction, as he refers to no destruction transmission. Brock-Fisher is transmitting twice down each beam ("ultrasound lines," col. 2, line 23) with a different transmit power each time. He then scales one received line linearly in proportion to the two transmit powers used. Finally, he subtracts the lines point-by-point. If there is no linear response at a point, the two should cancel. But if there is a nonlinear (harmonic) response from a point, the two echoes will not cancel but will leave a residual signal indicative of a nonlinearity of the point.

The Examiner discusses one approach Brock-Fisher uses to differentiate the power, which is to decrease the size of the transmit aperture (the number of transducer elements activated to transmit the beam) for the lower power line. But this is not the plane wave or beam area in the image field referred to in Claim 1. It is the number of elements of the array used for a transmit event. To the contrary, Brock-Fisher would want his beam profiles to be the same for each beam so that the two will completely cancel when there is no nonlinear response. Consequently there is no suggestion of transmitting with a plane wave of a large area and then imaging with smaller sized beams as called for by the present claimed invention. Brock-Fisher does not mention plane waves at all. This fact, together with the lack of any indication in Brock-Fisher that he is destroying microbubbles make

Brock-Fisher inapplicable to the present invention and thus it is respectfully submitted that Claim 1 and its dependent Claims 4 and 8 are patentable over Brock-Fisher and the prior art.

Claim 11 describes a method of obtaining an ultrasound perfusion image of tissues perfused with blood containing microbubbles, the method comprising using ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over a first area; and repetitively using ultrasound transmitted and received in a plurality of second areas that substantially encompasses the first area to obtain an indication of the quantity of microbubbles in the tissues that are intact over a re-perfusion time, each of the second areas being smaller than the first area, wherein the act of using ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over a first area comprises using a plane-wave beam of ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over the first area. As mentioned above, the prior art does not suggest using a plane wave to simultaneously destroy microbubbles in a large areas, then interrogate smaller areas that together comprise the large area to image reperfusion. Brock-Fisher gives no indication that he is destroying microbubbles at all, and only says that he is enhancing the detection of microbubbles with his two-line differentiation technique. Brock-Fisher's use of a smaller transmit aperture for the lower power transmit beam does not suggest any size difference between his transmitted beams. To the contrary, he is hoping that they will be the same so that the echoes will cancel when the relative powers are scaled. For these reasons it is respectfully submitted that Claim 11 and its dependent Claim 12 is patentable over Brock-Fisher and the prior art.

Claim 5 was rejected under 35 U.S.C. §103(a) as being unpatentable over US Pat. 6,340,348 (Krishnan) in view of Brock-Fisher and the prior art. Krishnan was cited for its teaching of the rapid transmission of destructive pulses, which was the focus of canceled Claim 3 and its dependent claims. Claim 5 has been amended to refer to plane waves and its dependency changed to Claim 1. Consequently it is respectfully submitted that Krishnan is no longer applicable to the claims of this case. Krishnan is not using plane waves, but individual transmit beams. See the abstract ("transmission of multiple beams of destruction pulses"); col. 4 line 65 ("destruction beams focused at different focal depths"); col. 4 lines 39-40 ("in order to destroy all the contrast agent along a given line"); and col. 7 line 11 ("transmit line spacing interval"). Accordingly it is respectfully submitted that Krishnan is using the same line-by-line technique referred to in the prior art section of the present application. Accordingly it is respectfully submitted that Claim 5 is patentable over the combination of Krishnan, Brock-Fisher, and the prior art.

Claim 7 was rejected under 35 U.S.C. §103(a) as being unpatentable over US Pat. 5,706,819 (Hwang et al.) in view of Brock-Fisher and the prior art. Hwang et al. was cited for its teaching of harmonic imaging. Hwang et al. is using a two-pulse technique for detecting harmonic (nonlinear) signals, and is separating the harmonics by a polarity or phase differentiation of the echoes from a point responsive to two differently modulated transmit pulses. Whereas Hwang et al. are using phase or polarity, Brock-Fisher is doing the same thing, harmonic separation, but with two-pulse transmit power differentiation. Hwang et al., like Brock-Fisher, does not show or suggest the use of plane waves, and he is involved in harmonic detection and separation (like Brock-Fisher), not microbubble destruction. For all of these reasons it is respectfully submitted that Claim 1 and its dependent Claim 7 are patentable over the combination of Hwang et al., Brock-Fisher, and the prior art.

In view of the foregoing discussion it is respectfully submitted that the present drawings are acceptable under Rule 437, that the title is now accurate, that Claim 5, is clear and definite, that Claims 1, 4, 8, 11 and 12 are patentable over Brock-Fisher and the prior art, that Claim 5 is patentable over Krishnan, Brock-Fisher and the prior art, and that Claim 7 is patentable over Hwang et al., Brock-Fisher and the prior art. Accordingly it is respectfully requested that the objection to the drawings be withdrawn, and that the rejection of Claim 5 under 35 U.S.C. §112, and the rejection of Claims 1, 4, 5, 7, 8, 11 and 12 under 35 U.S.C. §103(a) be withdrawn.

In light of the foregoing remarks, it is respectfully submitted that this application is now in condition for allowance. Favorable reconsideration is respectfully requested.

Respectfully submitted,

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July 16, 2009